

# NMCP COVID-19 Literature Report #50: Friday, 04 December 2020

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**Purpose:** These weekly reports, published on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers and leadership. All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

**Disclaimer:** I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

## Statistics

*Global today:* 65,408,787 confirmed cases and 1,509,743 deaths in 191 countries/regions

*1 week ago:* NA (no report last week)

*2 weeks ago:* 57,076,577 confirmed cases and 1,364,073 deaths in 191 countries/regions

### United States\*

top 5 states by cases (Virginia is ranked 19th)

	TOTAL US	CA	TX	FL	IL	NY
Cases	14,160,405	1,290,925	1,287,102	1,029,030	759,562	674,093
Tests	197,409,766	24,474,642	11,017,447	12,735,220	10,806,364	19,965,134
Deaths	276,513	19,595	22,575	18,874	13,624	34,775

\*see [census.gov](https://census.gov) for current US Population data; NA: not all data available

[JHU CSSE](#) as of 1000 EDT 04 December 2020

<i>Virginia</i>	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	247,380	6,841	2,882	4,179	6,728	3,256	2,836	11,318
Hospitalizations	15,116	544	134	165	471	357	169	556
Deaths	4,160	81	25	55	92	71	80	116

[VA DOH](#) as of 1000 EDT 04 December 2020

## From the CDC

The CDC released new guidance on quarantine:

"Henry Walke, MD, the CDC's COVID-19 incident manager, said though the 14-day quarantine period after exposure to COVID-19 is still ideal, the CDC now recommends two acceptable periods: 10 days without a test if the person in quarantine has no symptoms and 7 days with a negative test if the individual has no symptoms. In both instances, the CDC urges people to continue to monitor their symptoms for the full 14 days following exposure.

John Brooks, MD, chief medical officer for the CDC's COVID-19 response, said the new quarantine recommendations are based on extensive modeling in and outside the CDC and that the residual risk for the 10-day period ranges from 1% to 12%, with the residual risk for the 7-day period ranging from 5% to 10%.

He said the CDC has heard anecdotal reports from public health workers that many people aren't observing the ideal 14-day quarantine period, partly due to the need to go back to work. Brooks added that the agency hopes the shorter quarantine options will lead to better compliance and could even make people more willing share the names of their contacts with contact tracers." ([CIDRAP](#))

See: ["when to quarantine" guidance](#) (updated 02 December 2020)

The CDC also updated travel guidance:

"The CDC recommends that, if people decide to travel, they get tested 1 to 3 days before travel, with testing repeated 3 to 5 days after travel. For returning travelers, the CDC recommends they avoid nonessential activities for 7 days after travel for people who were tested, extending the period to 10 days for those who weren't tested." ([CIDRAP](#))

See: ["domestic travel during the COVID-19 pandemic" guidance](#) (updated 02 December 2020)

## Other Updates and Special Reports

NIH: [COVID-19 Treatment Guidelines](#) (updated 02 December 2020)

"On November 21, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) to make the casirivimab plus imdevimab combination available for the treatment of nonhospitalized patients with mild to moderate COVID-19 who are at high risk for progressing to severe disease and/or hospitalization. After reviewing the available evidence, the Panel has determined the following:

- At this time, there are insufficient data to recommend either for or against the use of casirivimab plus imdevimab for the treatment of outpatients with mild to moderate COVID-19.
- The casirivimab plus imdevimab combination should not be considered the standard of care for the treatment of patients with COVID-19.
- Health care providers are encouraged to discuss participation in severe acute respiratory syndrome coronavirus 2 neutralizing antibody clinical trials with patients who have mild to moderate COVID-19.
- Given the possibility of a limited supply of the casirivimab plus imdevimab combination, as well as challenges distributing and administering the drugs, patients at highest risk for COVID-19 progression should be prioritized for use of the drugs through the EUA. In addition, efforts should be made to ensure that the communities that are most affected by COVID-19 have equitable access to casirivimab plus imdevimab.
- Casirivimab plus imdevimab should not be withheld from a pregnant individual who has a condition that poses a high risk of progression to severe COVID-19, if the clinician thinks that the potential benefit of the drugs outweighs the potential risk.
- Patients who are hospitalized for COVID-19 should not receive casirivimab plus imdevimab outside of a clinical trial.
- There are currently no comparative data to determine whether there are differences in clinical efficacy or safety between casirivimab plus imdevimab and bamlanivimab."

For more details, see the statement: [The COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of the Casirivimab Plus Imdevimab Combination for the Treatment of COVID-19](#)

GAO: [COVID-19: Urgent Actions Needed to Better Ensure an Effective Federal Response](#) (released 30 November 2020)

"Our oversight of the federal COVID-19 response continues. Findings include:

- In our national survey, states and territories were concerned about ongoing shortages of some testing-related and other medical supplies (e.g., nitrile gloves)
- As vaccines and therapeutics are approved for use, more transparency around FDA's scientific reviews of safety and effectiveness is needed to strengthen public confidence in them
- HHS and CDC have provided little scientific explanation for changing key testing guidelines during the pandemic

In our report, we made [11 recommendations](#) and one suggestion for Congress to consider."

JHCHS: [Crisis Standards of Care: Lessons from New York City Hospitals' COVID-19 Experience](#) (24 November 2020)

"The purpose of this project was to convene a forum in which critical care physicians from a number of hospitals across New York City could frankly discuss their experiences with implementation of crisis standards of care (CSC). The Johns Hopkins Center for Health Security, in collaboration with New York City Health + Hospitals, convened a virtual working group in October 2020 consisting of 15 New York City intensive care unit (ICU) directors. The following major themes emerged from the discussion:

- Prepandemic CSC planning did not always align with the realities and clinical needs of the pandemic as it unfolded.
- The COVID-19 surge response was effective but often chaotic.
- Interhospital collaboration was an effective adaptive response.
- Situational awareness, especially related to information about patient load and resource availability, was a challenge for many clinicians.
- Multiple CSC challenges had to be overcome, especially around decision making for triage or allocation of life-sustaining care.
- Healthcare workers were profoundly psychologically affected by dealing with CSC issues amid the extraordinary surge."

### **Selected Literature: Peer-Reviewed Journals**

*Date given is the date published or posted online; often these papers are ahead of print.*

04 December 2020

MMWR: [Disproportionate Incidence of COVID-19 Infection, Hospitalizations, and Deaths Among Persons Identifying as Hispanic or Latino — Denver, Colorado March–October 2020](#)

"Racial and ethnic disparities of COVID-19 have been noted at the national level, but community-level data are limited.

In Denver, Colorado, the majority of adult COVID-19 cases (55%), hospitalizations (62%), and deaths (51%) were among Hispanic adults, double the proportion of Hispanic adults in Denver (24.9%). Among adults with COVID-19, Hispanic persons reported larger household sizes and more known COVID-19 household exposure, working in essential industries, working while ill, and delays in testing after symptom onset.

Public health, health systems, and social services need to address systemic inequalities to mitigate the disproportionate incidence of COVID-19 in Hispanic persons."

03 December 2020

JAMA Psychiatry: [Overdose-Related Cardiac Arrests Observed by Emergency Medical Services During the US COVID-19 Epidemic](#)

"This cohort study characterizes emergent trends in overdose-related cardiac arrests in the US during the coronavirus disease 2019 (COVID-19) pandemic using a large, national emergency medical services database."

MMWR: [The Advisory Committee on Immunization Practices' Interim Recommendation for Allocating Initial Supplies of COVID-19 Vaccine — United States, 2020](#)

"Demand is expected to exceed supply during the first months of the national COVID-19 vaccination program.

The Advisory Committee on Immunization Practices (ACIP) recommended, as interim guidance, that both 1) health care personnel and 2) residents of long-term care facilities be offered COVID-19 vaccine in the initial phase of the vaccination program.

Federal, state, and local jurisdictions should use this guidance for COVID-19 vaccination program planning and implementation. ACIP will consider vaccine-specific recommendations and additional populations when a Food and Drug Administration–authorized vaccine is available."

02 December 2020

Emerg Infect Dis: [COVID-19 and infant hospitalizations for seasonal respiratory virus infections, New Zealand, 2020](#)

"In March 2020, a national elimination strategy for coronavirus disease was introduced in New Zealand. Since then, hospitalizations for lower respiratory tract infection among infants <2 years of age and cases of respiratory syncytial or influenza virus infection have dramatically decreased. These findings indicate additional benefits of coronavirus disease control strategies."

Health Aff: [Increased Intensity Of PCR Testing Reduced COVID-19 Transmission Within Countries During The First Pandemic Wave](#)

"Experts agree that reverse transcription–polymerase chain reaction (PCR) testing is critical in controlling coronavirus disease 2019 (COVID-19), but decision-makers disagree on how much testing is optimal. Controlling for interventions and ecological factors, we used linear regression to quantify testing's impact on COVID-19's average reproduction number, representing transmissibility, in 173 countries and territories, accounting for 99% of the world's COVID-19 cases, during March to June 2020. Amongst interventions, PCR testing

had the greatest influence—a ten-fold increase in the ratio of tests to new cases reported reduced the average reproduction number by 9% across a range of testing levels. Our results imply that mobility reductions (e.g., shelter-in-place orders) were less effective in developing countries than in developed countries. Our results help explain how some nations achieved near-elimination of COVID-19 and the failure of lockdowns to slow COVID-19 in others. Our findings suggest that World Health Organization and other testing benchmarks are insufficient for COVID-19 control. Increased testing and isolation may represent the most effective, least costly alternative in terms of money, economic growth and human life for controlling COVID-19."

JACC Case Rep: [Reversible Myocardial Injury Associated With SARS-CoV-2 in an Infant](#)

"Coronavirus disease-2019 is caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) and has been associated with myocardial dysfunction and heart failure in adult patients. We report a case of reversible myocardial injury and heart failure in an infant with SARS-CoV-2 infection."

NEJM: [Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results](#)

"World Health Organization expert groups recommended mortality trials of four repurposed antiviral drugs — remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a — in patients hospitalized with coronavirus disease 2019 (Covid-19).

We randomly assigned inpatients with Covid-19 equally between one of the trial drug regimens that was locally available and open control (up to five options, four active and the local standard of care). The intention-to-treat primary analyses examined in-hospital mortality in the four pairwise comparisons of each trial drug and its control (drug available but patient assigned to the same care without that drug). Rate ratios for death were calculated with stratification according to age and status regarding mechanical ventilation at trial entry.

At 405 hospitals in 30 countries, 11,330 adults underwent randomization; 2750 were assigned to receive remdesivir, 954 to hydroxychloroquine, 1411 to lopinavir (without interferon), 2063 to interferon (including 651 to interferon plus lopinavir), and 4088 to no trial drug. Adherence was 94 to 96% midway through treatment, with 2 to 6% crossover. In total, 1253 deaths were reported (median day of death, day 8; interquartile range, 4 to 14). The Kaplan–Meier 28-day mortality was 11.8% (39.0% if the patient was already receiving ventilation at randomization and 9.5% otherwise). Death occurred in 301 of 2743 patients receiving remdesivir and in 303 of 2708 receiving its control (rate ratio, 0.95; 95% confidence interval [CI], 0.81 to 1.11; P=0.50), in 104 of 947 patients receiving hydroxychloroquine and in 84 of 906 receiving its control (rate ratio, 1.19; 95% CI, 0.89 to 1.59; P=0.23), in 148 of 1399 patients receiving lopinavir and in 146 of 1372 receiving its control (rate ratio, 1.00; 95% CI, 0.79 to 1.25; P=0.97), and in 243 of 2050 patients receiving

interferon and in 216 of 2050 receiving its control (rate ratio, 1.16; 95% CI, 0.96 to 1.39;  $P=0.11$ ). No drug definitely reduced mortality, overall or in any subgroup, or reduced initiation of ventilation or hospitalization duration.

These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay."

*01 December 2020*

Ann Intern Med: [Racial and Ethnic Disparities in COVID-19-Related Infections, Hospitalizations, and Deaths : A Systematic Review](#)

"Background: Data suggest that the effects of coronavirus disease 2019 (COVID-19) differ among U.S. racial/ethnic groups.

Purpose: To evaluate racial/ethnic disparities in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection rates and COVID-19 outcomes, factors contributing to disparities, and interventions to reduce them. (PROSPERO: CRD42020187078).

Data sources: English-language articles in MEDLINE, PsycINFO, CINAHL, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Scopus, searched from inception through 31 August 2020. Gray literature sources were searched through 2 November 2020.

Study selection: Observational studies examining SARS-CoV-2 infections, hospitalizations, or deaths by race/ethnicity in U.S. settings.

Data extraction: Single-reviewer abstraction confirmed by a second reviewer; independent dual-reviewer assessment of quality and strength of evidence.

Data synthesis: 37 mostly fair-quality cohort and cross-sectional studies, 15 mostly good-quality ecological studies, and data from the Centers for Disease Control and Prevention and APM Research Lab were included. African American/Black and Hispanic populations experience disproportionately higher rates of SARS-CoV-2 infection, hospitalization, and COVID-19-related mortality compared with non-Hispanic White populations, but not higher case-fatality rates (mostly reported as in-hospital mortality) (moderate- to high-strength evidence). Asian populations experience similar outcomes to non-Hispanic White populations (low-strength evidence). Outcomes for other racial/ethnic groups have been insufficiently studied. Health care access and exposure factors may underlie the observed disparities more than susceptibility due to comorbid conditions (low-strength evidence).



Limitations: Selection bias, missing race/ethnicity data, and incomplete outcome assessments in cohort and cross-sectional studies must be considered. In addition, adjustment for key demographic covariates was lacking in ecological studies.

Conclusion: African American/Black and Hispanic populations experience disproportionately higher rates of SARS-CoV-2 infection and COVID-19-related mortality but similar rates of case fatality. Differences in health care access and exposure risk may be driving higher infection and mortality rates."

Int J Infect Dis: [Unique pattern of COVID-19 infection in the State of Hawai'i](#)

"This is a brief report of an unusual observation of COVID-19 infection in Hawaii. The State of Hawaii is one of the most remote of the Pacific islands with approximately 1.4 million persons. The racial and ethnic diversity is enormous. For example, the white Caucasians make up ~25%, Asians including Japanese, Chinese and other Asians ~30%, Hawaiians 20%. Pacific Islanders, mostly from Micronesia and Samoa, comprise ~4%.

We discovered that COVID-19 population rates in this group were up to 10 times the rate in all the others together and made up almost 30% of cases. This unique pattern is illustrated in the only figure. Moreover, we are unaware of COVID-19 transmission from the Pacific Islanders to the other island ethnicities. It is an epidemic within an epidemic in the Island."

MMWR: [Increase in Hospital-Acquired Carbapenem-Resistant \*Acinetobacter baumannii\* Infection and Colonization in an Acute Care Hospital During a Surge in COVID-19 Admissions — New Jersey, February–July 2020](#)

"Carbapenem-resistant *Acinetobacter baumannii* (CRAB) causes health care–associated infections that are challenging to contain and often linked to infection prevention and control (IPC) breaches.

A New Jersey hospital reported a cluster of 34 CRAB cases that peaked during a surge in COVID-19 hospitalizations. Strategies to preserve continuity of care led to deviations in IPC practices; CRAB cases decreased when normal operations resumed.

Hospitals managing surges of patients with COVID-19 might be vulnerable to outbreaks of multidrug-resistant organism (MDRO) infections. Maintaining IPC best practices (e.g., MDRO surveillance and hand hygiene and environmental cleaning audits) to the extent possible could mitigate spread."

30 November 2020

Clin Infect Dis: [Serologic testing of U.S. blood donations to identify SARS-CoV-2-reactive antibodies: December 2019-January 2020](#)



"SARS-CoV-2, the virus that causes COVID-19 disease, was first identified in Wuhan, China in December 2019, with subsequent worldwide spread. The first U.S. cases were identified in January 2020.

To determine if SARS-CoV-2 reactive antibodies were present in sera prior to the first identified case in the U.S. on January 19, 2020, residual archived samples from 7,389 routine blood donations collected by the American Red Cross from December 13, 2019 to January 17, 2020, from donors resident in nine states (California, Connecticut, Iowa, Massachusetts, Michigan, Oregon, Rhode Island, Washington, and Wisconsin) were tested at CDC for anti-SARS-CoV-2 antibodies. Specimens reactive by pan-immunoglobulin (pan Ig) enzyme linked immunosorbent assay (ELISA) against the full spike protein were tested by IgG and IgM ELISAs, microneutralization test, Ortho total Ig S1 ELISA, and receptor binding domain / Ace2 blocking activity assay.

Of the 7,389 samples, 106 were reactive by pan Ig. Of these 106 specimens, 90 were available for further testing. Eighty four of 90 had neutralizing activity, 1 had S1 binding activity, and 1 had receptor binding domain / Ace2 blocking activity >50%, suggesting the presence of anti-SARS-CoV-2-reactive antibodies. Donations with reactivity occurred in all nine states.

These findings suggest that SARS-CoV-2 may have been introduced into the United States prior to January 19, 2020."

Emerg Infect Dis: [Absence of SARS-CoV-2 transmission from children in isolation to guardians, South Korea](#)

"We explored transmission of severe acute respiratory syndrome coronavirus 2 among 12 children and their uninfected guardians in hospital isolation rooms in South Korea. We found that, even with close frequent contact, guardians who used appropriate personal protective equipment were not infected by children with diagnosed coronavirus disease."

Emerg Infect Dis: [Childcare Exposure to Severe Acute Respiratory Syndrome Coronavirus 2 for 4-Year-Old Presymptomatic Child, South Korea](#)

"Data on transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from preschool-age children to children and adults are limited. We investigated SARS-CoV-2 exposure at a childcare center in South Korea. A 4-year-old child, probably infected by his grandmother, attended the center during the presymptomatic period (February 19–21, 2020). Fever developed on February 22, and he was given a diagnosis SARS-CoV-2 infection on February 27. At the center, 190 persons (154 children and 36 adults) were identified as contacts; 44 (23.2%) were defined as close contacts (37 children and 7 adults). All 190 persons were negative for SARS-CoV-2 on days 8–9 after the last exposure. Two close contacts (1 child and 1 adult) showed development of symptoms on the last day of

quarantine. However, subsequent test results were negative. This investigation adds indirect evidence of low potential infectivity in a childcare setting with exposure to a presymptomatic child."

J Korean Med Sci: [Evidence of Long-Distance Droplet Transmission of SARS-CoV-2 by Direct Air Flow in a Restaurant in Korea](#)

"The transmission mode of severe acute respiratory syndrome coronavirus 2 is primarily known as droplet transmission. However, a recent argument has emerged about the possibility of airborne transmission. On June 17, there was a coronavirus disease 2019 (COVID-19) outbreak in Korea associated with long distance droplet transmission.

The epidemiological investigation was implemented based on personal interviews and data collection on closed-circuit television images, and cell phone location data. The epidemic investigation support system developed by the Korea Disease Control and Prevention Agency was used for contact tracing. At the restaurant considered the site of exposure, air flow direction and velocity, distances between cases, and movement of visitors were investigated.

A total of 3 cases were identified in this outbreak, and maximum air flow velocity of 1.2 m/s was measured between the infector and infectee in a restaurant equipped with ceiling-type air conditioners. The index case was infected at a 6.5 m away from the infector and 5 minutes exposure without any direct or indirect contact.

Droplet transmission can occur at a distance greater than 2 m if there is direct air flow from an infected person. Therefore, updated guidelines involving prevention, contact tracing, and quarantine for COVID-19 are required for control of this highly contagious disease."

JAMA Netw Open: [Race/Ethnicity Among Children With COVID-19–Associated Multisystem Inflammatory Syndrome](#)

"This cohort study describes the distribution of race/ethnicity among cases of coronavirus disease 2019 (COVID-19)–associated multisystem inflammatory syndrome in children reported to the New York City Department of Health and Mental Hygiene."

Nat Neurosci: [Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19](#)

"The newly identified severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19, a pandemic respiratory disease. Moreover, thromboembolic events throughout the body, including in the CNS, have been described. Given the neurological symptoms observed in a large majority of individuals with COVID-19, SARS-CoV-2 penetrance of the CNS is likely. By various means, we demonstrate the presence of SARS-CoV-2 RNA and protein in anatomically distinct regions of the nasopharynx and brain. Furthermore, we

describe the morphological changes associated with infection such as thromboembolic ischemic infarction of the CNS and present evidence of SARS-CoV-2 neurotropism. SARS-CoV-2 can enter the nervous system by crossing the neural–mucosal interface in olfactory mucosa, exploiting the close vicinity of olfactory mucosal, endothelial and nervous tissue, including delicate olfactory and sensory nerve endings. Subsequently, SARS-CoV-2 appears to follow neuroanatomical structures, penetrating defined neuroanatomical areas including the primary respiratory and cardiovascular control center in the medulla oblongata."

Sci Transl Med: [Lung transplantation for patients with severe COVID-19](#)

"Lung transplantation can potentially be a life-saving treatment for patients with non-resolving COVID-19-associated respiratory failure. Concerns limiting lung transplantation include recurrence of SARS-CoV-2 infection in the allograft, technical challenges imposed by viral-mediated injury to the native lung, and the potential risk for allograft infection by pathogens causing ventilator-associated pneumonia in the native lung. Importantly, the native lung might recover, resulting in long-term outcomes preferable to those of transplant. Here, we report the results of lung transplantation in three patients with non-resolving COVID-19-associated respiratory failure.

We performed single molecule fluorescent in situ hybridization (smFISH) to detect both positive and negative strands of SARS-CoV-2 RNA in explanted lung tissue from the three patients and in additional control lung tissue samples. We conducted extracellular matrix imaging and single cell RNA sequencing on explanted lung tissue from the three patients who underwent transplantation and on warm post-mortem lung biopsies from two patients who had died from COVID-19-associated pneumonia. Lungs from these five patients with prolonged COVID-19 disease were free of SARS-CoV-2 as detected by smFISH, but pathology showed extensive evidence of injury and fibrosis that resembled end-stage pulmonary fibrosis. Using machine learning, we compared single cell RNA sequencing data from the lungs of patients with late stage COVID-19 to that from the lungs of patients with pulmonary fibrosis and identified similarities in gene expression across cell lineages.

Our findings suggest that some patients with severe COVID-19 develop fibrotic lung disease for which lung transplantation is their only option for survival."

29 November 2020

J Infect Dis: [Outdoor Transmission of SARS-CoV-2 and Other Respiratory Viruses, a Systematic Review](#)

"We conducted a systematic review of peer-reviewed papers indexed in PubMed, EMBASE and Web of Science and pre-prints in Europe PMC through August 12 th, 2020 that

described cases of human transmission of SARS-CoV-2. Reports of other respiratory virus transmission were included for reference.

Five identified studies found that a low proportion of reported global SARS-CoV-2 infections have occurred outdoors (<10%) and the odds of indoor transmission was very high compared to outdoors (18.7 times; 95% CI 6.0, 57.9). Five studies described influenza transmission outdoors and two described adenovirus transmission outdoors. There was high heterogeneity in study quality and individual definitions of outdoor settings which limited our ability to draw conclusions about outdoor transmission risks. In general, factors such as duration and frequency of personal contact, lack of personal protective equipment and occasional indoor gathering during a largely outdoor experience were associated with outdoor reports of infection.

Existing evidence supports the wide-held belief that the the risk of SARS-CoV-2 transmission is lower outdoors but there are significant gaps in our understanding of specific pathways."

*27 November 2020*

Br J Clin Pharmacol: [Clinical studies assessing the efficacy, effectiveness, and safety of remdesivir in management of COVID-19: a scoping review](#)

"Our scoping review searched Pubmed, Embase (Ovid), Scopus, and 17 primary trial registries for empirical publications or active registered clinical trials for data on the efficacy, effectiveness, or safety of remdesivir for COVID-19 or SARS-CoV-2. We conducted a narrative synthesis of the included publications.

17 empirical studies and 23 clinical trial registrations (n=40) accumulated 46,508 participants. We found four published randomised controlled trials accumulating 2,293 patients. Two trials reported shorter median recovery time and better clinical status among patients who received remdesivir compared with the control groups. Observational studies report an association between remdesivir treatment and decreased mortality, as well as increased survival. The most common adverse reaction was hepatic impairment, although the trials reported a similar proportion of adverse events in the intervention and control groups.

Remdesivir might shorten the time to clinical improvement among hospitalized adults with severe COVID-19. Trial data report a similar proportion of adverse events in treated and control groups. The results of the 23 registered active trials, including more than 30,000 participants, will shed light on the efficacy and safety of the antiviral. The findings of the remaining clinical trials expected to report results in 2020 will allow a quantitative synthesis of available evidence."

MMWR: [The Advisory Committee on Immunization Practices' Ethical Principles for Allocating Initial Supplies of COVID-19 Vaccine — United States, 2020](#)

"During the period when the U.S. supply of COVID-19 vaccines is limited, the Advisory Committee on Immunization Practices (ACIP) will make vaccine allocation recommendations.

In addition to scientific data and implementation feasibility, four ethical principles will assist ACIP in formulating recommendations for the initial allocation of COVID-19 vaccine: 1) maximizing benefits and minimizing harms; 2) promoting justice; 3) mitigating health inequities; and 4) promoting transparency.

Ethical principles will aid ACIP in making vaccine allocation recommendations and state, tribal, local, and territorial public health authorities in developing vaccine implementation strategies based on ACIP's recommendations."

MMWR: [Decline in SARS-CoV-2 Antibodies After Mild Infection Among Frontline Health Care Personnel in a Multistate Hospital Network — 12 States, April–August 2020](#)

"Most persons develop virus-specific antibodies to SARS-CoV-2 after infection; however, the timeline of antibody decline over time is uncertain.

Among 156 frontline health care personnel who had positive SARS-CoV-2 antibody test results in spring 2020, 94% experienced a decline at repeat testing approximately 60 days later, and 28% seroreverted to below the threshold of positivity. Participants with higher initial antibody responses were more likely to have antibodies detected at the follow-up test than were those who had a lower initial antibody response.

SARS-CoV-2 antibodies decline over weeks following acute infection. Negative SARS-CoV-2 serologic results do not exclude previous infection, which has significant impacts on how serologic studies are interpreted."

*26 November 2020*

Open Forum Infect Dis: [Clinical symptoms among ambulatory patients tested for SARS-CoV-2](#)

"We compared symptoms and characteristics of 4961 ambulatory patients with and without laboratory-confirmed SARS-CoV-2 infection. Findings indicate that clinical symptoms alone would be insufficient to distinguish between COVID-19 and other respiratory infections (e.g., influenza) and/or to evaluate the effects of preventive interventions (e.g., vaccinations)."

Sci Rep: [COVID-19 predictability in the United States using Google Trends time series](#)

"During the unprecedented situation that all countries around the globe are facing due to the Coronavirus disease 2019 (COVID-19) pandemic, which has also had severe socioeconomic consequences, it is imperative to explore novel approaches to monitoring and forecasting regional outbreaks as they happen or even before they do so. To that end, in this paper, the role of Google query data in the predictability of COVID-19 in the United States at both national and state level is presented. As a preliminary investigation, Pearson and Kendall rank correlations are examined to explore the relationship between Google Trends data and COVID-19 data on cases and deaths. Next, a COVID-19 predictability analysis is performed, with the employed model being a quantile regression that is bias corrected via bootstrap simulation, i.e., a robust regression analysis that is the appropriate statistical approach to taking against the presence of outliers in the sample while also mitigating small sample estimation bias. The results indicate that there are statistically significant correlations between Google Trends and COVID-19 data, while the estimated models exhibit strong COVID-19 predictability. In line with previous work that has suggested that online real-time data are valuable in the monitoring and forecasting of epidemics and outbreaks, it is evident that such infodemiology approaches can assist public health policy makers in addressing the most crucial issues: flattening the curve, allocating health resources, and increasing the effectiveness and preparedness of their respective health care systems."

25 November 2020

BMC Med: [Evidence for treatment with estradiol for women with SARS-CoV-2 infection](#)

"Given that an individual's age and gender are strongly predictive of coronavirus disease 2019 (COVID-19) outcomes, do such factors imply anything about preferable therapeutic options?

An analysis of electronic health records for a large (68,466-case), international COVID-19 cohort, in 5-year age strata, revealed age-dependent sex differences. In particular, we surveyed the effects of systemic hormone administration in women. The primary outcome for estradiol therapy was death. Odds ratios (ORs) and Kaplan-Meier survival curves were analyzed for 37,086 COVID-19 women in two age groups: pre- (15–49 years) and peri-/post-menopausal (> 50 years).

The incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is higher in women than men (by about + 15%) and, in contrast, the fatality rate is higher in men (about + 50%). Interestingly, the relationships between these quantities are linked to age: pre-adolescent girls and boys had the same risk of infection and fatality rate, while

adult premenopausal women had a significantly higher risk of infection than men in the same 5-year age stratum (about 16,000 vs. 12,000 cases). This ratio changed again in peri- and postmenopausal women, with infection susceptibility converging with men. While fatality rates increased continuously with age for both sexes, at 50 years, there was a steeper increase for men. Thus far, these types of intricacies have been largely neglected. Because the hormone 17 $\beta$ -estradiol influences expression of the human angiotensin-converting enzyme 2 (ACE2) protein, which plays a role in SARS-CoV-2 cellular entry, propensity score matching was performed for the women's sub-cohort, comparing users vs. non-users of estradiol. This retrospective study of hormone therapy in female COVID-19 patients shows that the fatality risk for women > 50 years receiving estradiol therapy (user group) is reduced by more than 50%; the OR was 0.33, 95% CI [0.18, 0.62] and the hazard ratio (HR) was 0.29, 95% CI [0.11, 0.76]. For younger, pre-menopausal women (15–49 years), the risk of COVID-19 fatality is the same irrespective of estradiol treatment, probably because of higher endogenous estradiol levels.

As of this writing, still no effective drug treatment is available for COVID-19; since estradiol shows such a strong improvement regarding fatality in COVID-19, we suggest prospective studies on the potentially more broadly protective roles of this naturally occurring hormone."

JAMA Dermatol: [Clinical, Laboratory, and Interferon-Alpha Response Characteristics of Patients With Chilblain-like Lesions During the COVID-19 Pandemic](#)

"Question: What are the clinical, pathologic, and laboratory characteristics of patients with chilblain-like lesions during the coronavirus 2019 (COVID-19) pandemic?

Findings: In this series of 40 consecutive patients with chilblain-like lesions, none had positive findings on polymerase chain reaction (PCR) tests, and 12 (30%) had positive COVID-19 serologic results. Common findings included increased D-dimers, lymphocytic inflammation, vascular damage on skin biopsy results, and a significant interferon-alpha response compared with patients with PCR-positive, acute COVID-19 infection.

Meaning: Patients presenting with chilblain-like lesions during the COVID-19 pandemic all had negative PCR results for COVID-19 at the time of the diagnosis and developed antibodies in only 30% of cases, and had histologic and biologic patterns of type I interferonopathy."

*24 November 2020*

Am Surg: [The Effects of the COVID-19 Pandemic on Trauma Presentations in a Level One Trauma Center](#)



"Over 28 million confirmed cases of COVID-19 have been reported to date, resulting in over 900 000 deaths. With an increase in awareness regarding the virus, the behavior of general population has changed dramatically. As activities such as driving and hospital presentation patterns have changed, our study aimed to assess the differences in trauma case variables before and during the COVID-19 pandemic.

Trauma data for the period of March 1st-June 15th were compared for the years 2015-2019 (pre-COVID) and 2020 (COVID). The data were analyzed across the following categories: injury severity score, injury mechanism, motor vehicle crashes (MVCs) vs. other blunt injuries, alcohol involvement, and length of hospital stay.

The median injury severity score pre-COVID and during COVID was 9, representing no change. There was no difference in overall distribution of mechanism of injury; however, there was a significant decrease in the percentage of MVCs pre-COVID (36.39%) vs. COVID (29.6%,  $P < .05$ ). Alcohol was significantly more likely to be involved in trauma during COVID-19 ( $P < .05$ ). The mean hospital stay increased from 3.87-5.4 days during COVID-19 ( $P < .05$ ).

We saw similar results to prior studies in terms of there being no change in trauma severity. Our observation that motor vehicle collisions have decreased is consistent with current data showing decreased use of motor vehicles during the pandemic. We also observed an increase in alcohol-related cases which are consistent with the reported changes in alcohol consumption since the pandemic began."

CMAJ: [Symptoms associated with a positive result for a swab for SARS-CoV-2 infection among children in Alberta](#)

"We conducted an observational study among children tested and followed for SARS-CoV-2 infection using nasal, nasopharyngeal, throat or other (e.g., nasopharyngeal aspirate or tracheal secretions, or unknown) swabs between Apr. 13 and Sept. 30, 2020, in Alberta. We calculated positive likelihood ratios (LRs) for self-reported symptoms and a positive SARS-CoV-2 swab result in the entire cohort and in 3 sensitivity analyses: all children with at least 1 symptom, all children tested because of contact tracing whether they were symptomatic or not and all children 5 years of age or older.

We analyzed results for 2463 children who underwent testing for SARS-CoV-2 infection; 1987 children had a positive result and 476 had a negative result. Of children with a positive test result for SARS-CoV-2, 714 (35.9%) reported being asymptomatic. Although cough (24.5%) and rhinorrhea (19.3%) were 2 of the most common symptoms among children with SARS-CoV-2 infection, they were also common among those with negative test results and were not predictive of a positive test (positive LR 0.96, 95% confidence interval [CI] 0.81–1.14, and 0.87, 95% CI 0.72–1.06, respectively). Anosmia/ageusia (positive LR 7.33, 95% CI 3.03–17.76), nausea/vomiting (positive LR 5.51, 95% CI 1.74–17.43), headache

(positive LR 2.49, 95% CI 1.74–3.57) and fever (positive LR 1.68, 95% CI 1.34–2.11) were the symptoms most predictive of a positive result for a SARS-CoV-2 swab. The positive LR for the combination of anosmia/ageusia, nausea/vomiting and headache was 65.92 (95% CI 49.48–91.92).

About two-thirds of the children who tested positive for SARS-CoV-2 infection reported symptoms. The symptoms most strongly associated with a positive SARS-CoV-2 swab result were anosmia/ageusia, nausea/vomiting, headache and fever."

JAMA Intern Med: [Estimated SARS-CoV-2 Seroprevalence in the US as of September 2020](#)

"Question: What proportion of persons across 52 US jurisdictions had detectable antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from July to September 2020?

Findings: In this repeated, cross-sectional study of 177 919 residual clinical specimens, the estimated percentage of persons in a jurisdiction with detectable SARS-CoV-2 antibodies ranged from fewer than 1% to 23%. Over 4 sampling periods in 42 of 49 jurisdictions with calculated estimates, fewer than 10% of people had detectable SARS-CoV-2 antibodies.

Meaning: While SARS-CoV-2 antibody prevalence estimates varied widely across jurisdictions, most people in the US did not have evidence of previous SARS-CoV-2 infection."

NEJM: [A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia](#)

"Convalescent plasma is frequently administered to patients with Covid-19 and has been reported, largely on the basis of observational data, to improve clinical outcomes. Minimal data are available from adequately powered randomized, controlled trials.

We randomly assigned hospitalized adult patients with severe Covid-19 pneumonia in a 2:1 ratio to receive convalescent plasma or placebo. The primary outcome was the patient's clinical status 30 days after the intervention, as measured on a six-point ordinal scale ranging from total recovery to death.

A total of 228 patients were assigned to receive convalescent plasma and 105 to receive placebo. The median time from the onset of symptoms to enrollment in the trial was 8 days (interquartile range, 5 to 10), and hypoxemia was the most frequent severity criterion for enrollment. The infused convalescent plasma had a median titer of 1:3200 of total SARS-CoV-2 antibodies (interquartile range, 1:800 to 1:3200). No patients were lost to follow-up. At day 30 day, no significant difference was noted between the convalescent plasma group and the placebo group in the distribution of clinical outcomes according to the ordinal scale (odds ratio, 0.83 (95% confidence interval [CI], 0.52 to 1.35; P=0.46). Overall mortality was 10.96% in the convalescent plasma group and 11.43% in the placebo group, for a risk

difference of -0.46 percentage points (95% CI, -7.8 to 6.8). Total SARS-CoV-2 antibody titers tended to be higher in the convalescent plasma group at day 2 after the intervention. Adverse events and serious adverse events were similar in the two groups.

No significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo."

Radiology: [DeepCOVID-XR: An Artificial Intelligence Algorithm to Detect COVID-19 on Chest Radiographs Trained and Tested on a Large US Clinical Dataset](#)

"DeepCOVID-XR, an artificial intelligence algorithm for detecting COVID-19 on chest radiographs, demonstrated performance similar to the consensus of experienced thoracic radiologists. Key Results:

- DeepCOVID-XR classified 2,214 test images (1,194 COVID-19 positive) with an accuracy of 83% and AUC of 0.90 compared with the reference standard of RT-PCR.
- On 300 random test images (134 COVID-19 positive), DeepCOVID-XR's accuracy was 82% (AUC 0.88) compared to 5 individual thoracic radiologists (accuracy 76%-81%) and the consensus of all 5 radiologists (accuracy 81%, AUC 0.85).
- Using the consensus interpretation of the radiologists as the reference standard, DeepCOVID-XR's AUC was 0.95."

*23 November 2020*

BMC Infect Dis: [Atypical presentation of COVID-19; an observational retrospective study](#)

"COVID-19 infection may present with atypical signs and symptoms and false negative polymerase chain reaction (PCR) tests predisposing healthy people and health care workers to infection. The aim of the current study is to evaluate the features of atypical presentations in COVID-19 infection in a referral center in Tehran, Iran.

Hospital database of inpatients admitted to Loghman Hakim hospital between February 20th and May 11th, 2020 was reviewed and all patients with final diagnosis of COVID-19 infection were evaluated for their presenting symptoms. Patients with chief complaints of "fever", "dyspnea", and/or "cough" as typical presentations of COVID-19 were excluded and those with other clinical presentations were included.

Nineteen patients were included with a mean age of  $51 \pm 19$  years, of whom, 17 were males (89%). Median [IQR] Glasgow coma scale (GCS) was 14 [13, 15]. Almost 10 had referred with chief complaint of methanol poisoning and overdose on substances of abuse. Only 8 cases (42%) had positive COVID-19 test. Nine (47%) needed invasive mechanical ventilation, of

whom, two had positive COVID-19 test results ( $p = ns$ ). Eight patients (42%) died with three of them having positive PCRs.

In patients referring to emergency departments with chief complaint of poisoning (especially poisonings that can result in dyspnea including substances of abuse and toxic alcohols), gastrointestinal, and constitutional respiratory symptoms, attention should be given not to miss possible cases of COVID-19."

Crit Care: [Dosing of thromboprophylaxis and mortality in critically ill COVID-19 patients](#)

"In this retrospective study, all critically ill COVID-19 patients admitted to two intensive care units in March and April 2020 were eligible. Patients were categorized into three groups according to initial daily dose of thromboprophylaxis: low (2500–4500 IU tinzaparin or 2500–5000 IU dalteparin), medium ( $> 4500$  IU but  $< 175$  IU/kilogram, kg, of body weight tinzaparin or  $> 5000$  IU but  $< 200$  IU/kg of body weight dalteparin), and high dose ( $\geq 175$  IU/kg of body weight tinzaparin or  $\geq 200$  IU/kg of body weight dalteparin).

Thromboprophylaxis dosage was based on local standardized recommendations, not on degree of critical illness or risk of thrombosis. Cox proportional hazards regression was used to estimate hazard ratios with corresponding 95% confidence intervals of death within 28 days from ICU admission. Multivariable models were adjusted for sex, age, body mass index, Simplified Acute Physiology Score III, invasive respiratory support, and initial dosing strategy of thromboprophylaxis.

A total of 152 patients were included: 67 received low-, 48 medium-, and 37 high-dose thromboprophylaxis. Baseline characteristics did not differ between groups. For patients who received high-dose prophylaxis, mortality was lower (13.5%) compared to those who received medium dose (25.0%) or low dose (38.8%),  $p = 0.02$ . The hazard ratio of death was 0.33 (95% confidence intervals 0.13–0.87) among those who received high dose, and 0.88 (95% confidence intervals 0.43–1.83) among those who received medium dose, as compared to those who received low-dose thromboprophylaxis. There were fewer thromboembolic events in the high (2.7%) vs medium (18.8%) and low-dose thromboprophylaxis (17.9%) groups,  $p = 0.04$ .

Among critically ill COVID-19 patients with respiratory failure, high-dose thromboprophylaxis was associated with a lower risk of death and a lower cumulative incidence of thromboembolic events compared with lower doses."

JAMA: [Psychological Distress and COVID-19–Related Stressors Reported in a Longitudinal Cohort of US Adults in April and July 2020](#)

"This study used an online survey to assess how psychological distress has changed over the course of the coronavirus disease 2019 (COVID-19) pandemic from April to July 2020."

JAMA Pediatr: [Assessment of 135 794 Pediatric Patients Tested for Severe Acute Respiratory Syndrome Coronavirus 2 Across the United States](#)

"Question: What is the epidemiology across the United States of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among pediatric patients undergoing diagnostic testing for the virus?

Findings: In this cohort study using electronic health records for 135 794 US pediatric patients in 7 children's health systems, 96% of patients tested had negative results, and rates of severe cardiorespiratory presentation of coronavirus disease 2019 (COVID-19) illness were low. Minority race/ethnicity, chronic illness, and increasing age were associated with SARS-CoV-2 infection.

Meaning: This study suggests that for most pediatric patients, the risk of SARS-CoV-2 infection appears low, but higher concern may be warranted for patients with medically complex conditions or those of minority race/ethnicity."

PLoS One: [Outcomes of mechanically ventilated patients with COVID-19 associated respiratory failure](#)

"The outcomes of patients requiring invasive mechanical ventilation for COVID-19 remain poorly defined. We sought to determine clinical characteristics and outcomes of patients with COVID-19 managed with invasive mechanical ventilation in an appropriately resourced US health care system.

Outcomes of COVID-19 infected patients requiring mechanical ventilation treated within the Inova Health System between March 5, 2020 and April 26, 2020 were evaluated through an electronic medical record review.

1023 COVID-19 positive patients were admitted to the Inova Health System during the study period. Of these, 164 (16.0%) were managed with invasive mechanical ventilation. All patients were followed to definitive disposition. 70/164 patients (42.7%) had died and 94/164 (57.3%) were still alive. Deceased patients were older (median age of 66 vs. 55,  $p < 0.0001$ ) and had a higher initial d-dimer (2.22 vs. 1.31,  $p = 0.005$ ) and peak ferritin levels (2998 vs. 2077,  $p = 0.016$ ) compared to survivors. 84.3% of patients over 70 years old died in the hospital. Conversely, 67.4% of patients age 70 or younger survived to hospital discharge. Younger age, non-Caucasian race and treatment at a tertiary care center were all associated with survivor status.

Mortality of patients with COVID-19 requiring invasive mechanical ventilation is high, with particularly daunting mortality seen in patients of advanced age, even in a well-resourced health care system. A substantial proportion of patients requiring invasive mechanical ventilation were not of advanced age, and this group had a reasonable chance for recovery."

20 November 2020

mBio: [Analysis of Measles-Mumps-Rubella \(MMR\) Titers of Recovered COVID-19 Patients](#)

"The measles-mumps-rubella (MMR) vaccine has been theorized to provide protection against coronavirus disease 2019 (COVID-19). Our aim was to determine whether any MMR IgG titers are inversely correlated with severity in recovered COVID-19 patients previously vaccinated with MMR II. We divided 80 subjects into two groups, comparing MMR titers to recent COVID-19 severity levels. The MMR II group consisted of 50 subjects who would primarily have MMR antibodies from the MMR II vaccine, and a comparison group of 30 subjects consisted of those who would primarily have MMR antibodies from sources other than MMR II, including prior measles, mumps, and/or rubella illnesses. There was a significant inverse correlation ( $r_s = -0.71$ ,  $P < 0.001$ ) between mumps virus titers (mumps titers) and COVID-19 severity within the MMR II group. There were no significant correlations between mumps titers and severity in the comparison group, between mumps titers and age in the MMR II group, or between severity and measles or rubella titers in either group. Within the MMR II group, mumps titers of 134 to 300 arbitrary units (AU)/ml ( $n = 8$ ) were found only in those who were functionally immune or asymptomatic; all with mild symptoms had mumps titers below 134 AU/ml ( $n = 17$ ); all with moderate symptoms had mumps titers below 75 AU/ml ( $n = 11$ ); all who had been hospitalized and had required oxygen had mumps titers below 32 AU/ml ( $n = 5$ ). Our results demonstrate that there is a significant inverse correlation between mumps titers from MMR II and COVID-19 severity.

IMPORTANCE: COVID-19 has presented various paradoxes that, if understood better, may provide clues to controlling the pandemic, even before a COVID-19 vaccine is widely available. First, young children are largely spared from severe disease. Second, numerous countries have COVID-19 death rates that are as low as 1% of the death rates of other countries. Third, many people, despite prolonged close contact with someone who is COVID-19 positive, never test positive themselves. Fourth, nearly half of people who test positive for COVID-19 are asymptomatic. Some researchers have theorized that the measles-mumps-rubella (MMR) vaccine may be responsible for these disparities. The significance of our study is that it showed that mumps titers related to the MMR II vaccine are significantly and inversely correlated with the severity of COVID-19-related symptoms, supporting the theorized association between the MMR vaccine and COVID-19 severity."

*ICYMI (older than last 2 weeks)*

Lancet Microbe: [SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis](#) (published 19 November 2020)



"To our knowledge, this is the first systematic review and meta-analysis that has examined and compared the viral dynamics of the three highly pathogenic human coronaviruses: SARS-CoV-2, SARS-CoV, and MERS-CoV. The results provide a comprehensive understanding regarding their viral kinetics and duration of shedding. Mean SARS-CoV-2 RNA shedding duration was 17·0 days (maximum shedding duration 83 days) in upper respiratory tract, 14·6 days (maximum 59 days) in lower respiratory tract, 17·2 days (maximum 35 days) in stool, and 16·6 days (maximum 60 days) in serum samples. Pooled mean SARS-CoV-2 shedding duration was positively associated with age. No study detected live virus beyond day 9 of illness, despite persistently high viral loads. SARS-CoV-2 viral load in the upper respiratory tract appeared to peak in the first week of illness, whereas SARS-CoV and MERS-CoV peaked later. Several studies reported similar viral loads at the start of infection among asymptomatic and symptomatic patients infected with SARS-CoV-2; however, most studies demonstrated faster viral clearance in asymptomatic individuals, as also seen in MERS-CoV, suggesting a shorter infectious period but with similar potential transmissibility at the onset of infection.

Our study shows that despite evidence of prolonged SARS-CoV-2 RNA shedding in respiratory and stool samples, viable virus appears to be short-lived. Therefore, RNA detection cannot be used to infer infectiousness. High titres of SARS-CoV-2 are detected early in the disease course, with an early peak observed at the time of symptom onset to day 5 of illness; this finding probably explains the efficient spread of SARS-CoV-2 compared with SARS-CoV and MERS-CoV. This has important implications for SARS-CoV-2 transmission in the community and hospital setting, emphasising the importance of early case finding and prompt isolation as well as public education about the spectrum of illness. Our study shows that isolation practices should be commenced with the start of first symptoms, which can include mild and atypical symptoms, preceding typical symptoms of COVID-19 such as cough and fever. However, given the potential delays in isolation of patients, even the early detection and isolation strategy might not be fully effective in containing SARS-CoV-2."

Arch Suicide Res: [Suicide in the Time of COVID-19: Review and Recommendations](#) (published 17 November 2020)

"The coronavirus (COVID-19) pandemic presents us with unusual challenges to the global health system and economics. The pandemic may not have an immediate impact on suicide rates, however, given that it is likely to result in a confluence of risk factors for suicide and economic crisis, it is highly possibly that it will lead to increases in suicide rates in the long-run. Elderly persons are more likely to live alone, be socially isolated during COVID-19 and have physical health problems, which are risk factors for suicide. Young children and health professionals may also be population at risk. Isolation, quarantine and the economic crisis that follows may impact mental health significantly. The International Academy of Suicide Research (IASR) is an organization dedicated to promote high standards of research and



scholarship in the field of suicidal behaviour to support efforts to prevent suicide globally. This IASR's board position paper gives recommendations for suicide research during the COVID-10 pandemic. Clinical research has to be modified due to COVID-19 shutdown."

Intern Med J: [Renin–angiotensin system inhibition and risk of infection and mortality in COVID-19: a systematic review and meta-analysis](#) (published 16 November 2020)

"We performed a systematic review and meta-analysis to investigate whether RAS inhibitors increased the likelihood of a positive test or death/severe illness in patients with COVID-19.

A systematic search of MEDLINE, PubMed and EMBASE was conducted for studies stratified by the use of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB). Pooled analysis was performed using a random-effects model.

Seven trials of 73 122 patients were included. Overall, 16 624 (22.7%) patients had a positive COVID-19 test and 7892 (10.8%) were on a RAS inhibitor. RAS inhibitors were not associated with higher likelihood of a positive COVID-19 test result (odds ratio (OR) 0.97 (95% CI 0.97–1.05,  $P = 0.48$ ) with low heterogeneity. This was comparable when stratifying by use of each medication class. The use of RAS inhibitors was also not associated with mortality or severe illness (OR 0.89, 95% CI 0.73–1.07,  $P = 0.21$ ) with moderate heterogeneity.

Use of ACEI or ARB was not associated with a heightened susceptibility for a positive diagnosis of COVID-19. Furthermore, they were not associated with increased illness severity or mortality due to COVID-19. Randomised controlled trials are needed to address definitively the potential benefits or harms of RAS inhibitors in patients with COVID-19."

### **Selected Literature: Preprints**

*Preprints are found on preprint servers such as [arXiv](#), [bioRxiv](#), and [medRxiv](#); they are commonly used for biomedical research. Preprints may later be published in peer-reviewed journals.*

*Per medRxiv: "Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."*

medRxiv: [The impact of non-pharmaceutical interventions on the prevention and control of COVID-19 in New York City](#) (posted 03 December 2020)

"The emergence of coronavirus disease 2019 (COVID-19) has infected more than 37 million people worldwide. The control responses varied across countries with different outcomes in

terms of epidemic size and social disruption. In this study, we presented an age-specific susceptible-exposed-infected-recovery-death model that considers the unique characteristics of COVID-19 to examine the effectiveness of various non-pharmaceutical interventions (NPIs) in New York City (NYC). Numerical experiments from our model show that the control policies implemented in NYC reduced the number of infections by 72% (IQR 53-95), and the number of deceased cases by 76% (IQR 58-96) by the end of 2020, respectively. Among all the NPIs, social distancing for the entire population and the protection for the elderly in the public facilities is the most effective control measure in reducing severe infections and deceased cases. School closure policy may not work as effectively as one might expect in terms of reducing the number of deceased cases. Our simulation results provide novel insights into the city-specific implementation of NPIs with minimal social disruption considering the locations and population characteristics."

medRxiv: [International estimates of intended uptake and refusal of COVID-19 vaccines: A rapid systematic review and meta-analysis of large nationally representative samples](#) (posted 03 December 2020)

"Background: Widespread uptake of COVID-19 vaccines will be essential to extinguishing the COVID-19 pandemic. Vaccines have been developed in unprecedented time and hesitancy towards vaccination among the general population is unclear.

Methods: Systematic review and meta-analysis of studies using large nationally representative samples ( $n \geq 1000$ ) to examine the percentage of the population intending to vaccinate, unsure, or intending to refuse a COVID-19 vaccine when available. Generic inverse meta-analysis and meta-regression were used to pool estimates and examine time trends. PubMed, Scopus and pre-printer servers were searched from January-November, 2020. Registered on PROSPERO (CRD42020223132).

Findings: Twenty-eight nationally representative samples ( $n = 58,656$ ) from 13 countries indicate that as the pandemic has progressed, the percentage of people intending to vaccinate and refuse vaccination have been decreasing and increasing respectively. Pooled data from surveys conducted during June-October suggest that 60% (95% CI: 49% to 69%) intend to vaccinate and 20% (95% CI: 13% to 29%) intend to refuse vaccination, although intentions vary substantially between samples and countries ( $I^2 > 90\%$ ). Being female, younger, of lower income or education level and belonging to an ethnic minority group were consistently associated with being less likely to intend to vaccinate. Findings were consistent across higher vs. lower quality studies.

Interpretation: Intentions to be vaccinated when a COVID-19 vaccine becomes available have been declining globally and there is an urgent need to address social inequalities in vaccine hesitancy and promote widespread uptake of vaccines as they become available."

medRxiv: [Predicting patients with false negative SARS-CoV-2 testing at hospital admission: A retrospective multi-center study](#) (posted 02 December 2020)

**Importance** False negative SARS-CoV-2 tests can lead to spread of infection in the inpatient setting to other patients and healthcare workers. However, the population of patients with COVID who are admitted with false negative testing is unstudied.

**Objective** To characterize and develop a model to predict true SARS-CoV-2 infection among patients who initially test negative for COVID by PCR.

**Design** Retrospective cohort study.

**Setting** Five hospitals within the Yale New Haven Health System between 3/10/2020 and 9/1/2020. **Participants:** Adult patients who received diagnostic testing for SARS-CoV-2 virus within the first 96 hours of hospitalization.

**Exposure** We developed a logistic regression model from readily available electronic health record data to predict SARS-CoV-2 positivity in patients who were positive for COVID and those who were negative and never retested.

**Main Outcomes and Measures** This model was applied to patients testing negative for SARS-CoV-2 who were retested within the first 96 hours of hospitalization. We evaluated the ability of the model to discriminate between patients who would subsequently retest negative and those who would subsequently retest positive.

**Results** We included 31,459 hospitalized adult patients; 2,666 of these patients tested positive for COVID and 3,511 initially tested negative for COVID and were retested. Of the patients who were retested, 61 (1.7%) had a subsequent positive COVID test. The model showed that higher age, vital sign abnormalities, and lower white blood cell count served as strong predictors for COVID positivity in these patients. The model had moderate performance to predict which patients would retest positive with a test set area under the receiver-operator characteristic (ROC) of 0.76 (95% CI 0.70 - 0.83). Using a cutpoint for our risk prediction model at the 90th percentile for probability, we were able to capture 35/61 (57%) of the patients who would retest positive. This cutpoint amounts to a number-needed-to-retest range between 15 and 77 patients.

**Conclusion and Relevance** We show that a pragmatic model can predict which patients should be retested for COVID. Further research is required to determine if this risk model can be applied prospectively in hospitalized patients to prevent the spread of SARS-CoV-2 infections."

## Events and Presentations

- WHAT:** CDC COCA: The Impact of Telehealth on Health Equity from the Perspective of Large Healthcare Systems during the COVID-19 Pandemic
- WHEN:** Tuesday, 08 December 2020, 1400 – 1500 ET
- DETAILS:** During this COCA Call, presenters from Kaiser Permanente and the Veteran's Health Administration will discuss how telehealth has affected health equity in their patient populations before and during the COVID-19 pandemic. Topics to discuss include challenges and opportunities related to telehealth implementation. Presenters will share strategies to expand access that can reduce disparities and improve culturally responsive care to help achieve health equity within each organization. In addition, presenters from the Centers for Disease Control and Prevention (CDC) will share telehealth strategies that incorporate CDC's frameworks to Addressing Health Equity in Public Health Practice.
- Free CE available
- See: [https://emergency.cdc.gov/coca/calls/2020/callinfo\\_120820.asp](https://emergency.cdc.gov/coca/calls/2020/callinfo_120820.asp)

- WHAT:** Physician Well-Being: What's Changed and What's More Important than Ever in the Wake of COVID-19
- DETAILS:** Register to view recording at:  
<https://register.gotowebinar.com/recording/187486934540164875>
- PowerPoint [pdf]: <https://files.asprtracie.hhs.gov/documents/covid-19-and-healthcare-professional-stress-and-resilience-speaker-series-carr-and-ripp.pdf>
- Transcript [pdf]: <https://files.asprtracie.hhs.gov/documents/behavioral-health-speaker-series-carr-ripp-transcript.pdf>

## News in Brief

More grim milestones:

- > On Wednesday, 02 December 2020, 2,804 Americans died from COVID-19 – more than the number of people killed on 9/11 at the World Trade Center and the Pentagon combined – setting a new single-day high ([BI](#)).
- > On the same day, the US reported 100,226 people hospitalized for COVID-19 – this is the first time daily hospitalizations exceeded 100K ([COVID Tracking Project](#)).

The CDC's director warns 'the most difficult in the public health history of this nation' will be the next few months ([CNBC](#)).

Much of the data on the pandemic come from the work of volunteers ([BB](#)).

### *COVID Vaccines*

The UK is the first country to approve a coronavirus vaccine: Pfizer/BioNTech's vaccine, which is expected to receive EUA from the US FDA soon; the first vaccinations may start in days ([BBC](#)).

Moderna joins Pfizer in requesting EUA from the FDA for their COVID-19 vaccine ([Moderna](#)).

Fun fact about that Moderna vaccine: it was designed in just 2 days ([BI](#); see also [this essay that gives a broader context](#)).

After concerns were raised about and confusion regarding recent results from their vaccine study, AstraZeneca may conduct another trial ([Bloomberg](#); see [this Nature article](#) for discussion of the concerns raised about the results).

Altimmune is set to start their phase 1 trial of a single-dose intranasal COVID-19 vaccine ([Global Biodefense](#)).

Vaccine data and results are just beginning ([Atlantic](#)).

### *Vaccine Distribution*

OWS officials said they can "distribute enough to vaccinate 20 million (40 million doses) in December, followed by 30 million in January (60 million doses), and 50 million in February (100 million doses)" ([CIDRAP](#); see [full briefing video \[1 hr\] via Twitter](#)).

The director of supply, production, and distribution for OWS said any American who wants a COVID-19 vaccine will have one by June 2021 ([MIT Tech Rev](#)).

The problem may be more in people refusing to get a vaccine though ([WaPo](#)).

Children may be the last in line, and may not be vaccinated before the new school year ([WaPo](#)).

"Many trial volunteers got placebo vaccines. Do they now deserve the real ones?" ([NYT](#))

Here's how various countries rank per capita on number of secured doses for their citizens ([Nature](#)).

COVID-19 vaccines and the vaccine supply chain are threatened by hackers ([WaPo](#)), organized crime ([Interpol](#)), and terrorist / violent extremist groups ([UNICRI](#)).

### *Treatment and Therapies*

The FDA has issued EUA for the combination of casirivimab and imdevimab in adults and children over 12 years old for treatment of mild to moderate COVID-19 at risk of progressing into severe cases ([FDA](#); see also NIH COVID guidelines update, above, on its use).

The NIH is starting the fourth iteration of its Adaptive COVID-19 Treatment Trial (ACTT-4); patients will be randomized to either dexamethasone plus remdesivir or remdesivir plus baricitinib ([NIH](#)).

The Medical Letter has updated its treatment table (now a whopping 125 pages) of drugs and therapies being considered for COVID-19 ([TML \[pdf\]](#)).

### *Exposure, Testing, and Risks*

Research suggests that home evictions are associated with more than 10,000 deaths from COVID-19 ([NPR](#)).

"A Hawaii couple knew they had coronavirus before flying. They boarded a flight anyway and were arrested, police say." ([WaPo](#)).

Wondering how 700 epidemiologists are living right now and what they think is next? This article has you covered ([NYT](#)).

### *Thanks, Coronavirus*

We're past moral injury and burnout... healthcare workers and others are getting burnover ([STAT](#)).

"A revamped strategic national stockpile still can't match the pandemic's latest surge" ([NPR](#)).

Researchers are looking into the possible link between COVID delirium and permanent cognitive decline ([Nature](#)).

A new report on student learning suggests the pandemic has slowed learning in math but little impact reading growth ([NPR](#); see [full report \[pdf\]](#)).

"The US could have hundreds of thousands of fewer births next year than it would have in the absence of a pandemic" ([Atlantic](#)).

Ambulance companies are yet another victim in the pandemic; their professional association told HHS that 'the 911 emergency medical system throughout the United States is at a breaking point' ([NBC](#)).



### *A Thousand Words*

"These are iPad stations being prepared for virtual ICU end of life visits by a palliative care doc I know. Jesus." ([Twitter](#); image used without permission).



### *Long Reads*

"The Wuhan files: leaked documents reveal China's mishandling of the early stages of COVID-19" ([CNN](#)).

"'Nobody sees us': testing-lab workers strain under demand" ([NYT](#)).

"Children of quarantine: what does a year of isolation and anxiety do to a developing brain?" ([Cut](#)).

"I'm 33 years old. I got COVID-19 eight months ago. I'm still sick." ([BFN](#))

"The Covid-19 vaccines are a marvel of science. Here's how we can make the best use of them" ([STAT](#)).



"Politics, science and the remarkable race for a coronavirus vaccine: The furious race to develop a coronavirus vaccine played out against a presidential election, between a pharmaceutical giant and a biotech upstart, with the stakes as high as they could get." ([NYT](#))

A bit of history: "We're celebrating Thanksgiving amid a pandemic. Here's how we did it in 1918 – and what happened next" ([USA Today](#)).

#### *Other Outbreaks and Health Threats*

This seems ominous, given 2020 so far: "coronaviruses closely related to the pandemic virus discovered in Japan and Cambodia" ([Nature](#)).

A year after the 2014 outbreak, 22.5% of healthcare workers in the DRC had Ebola virus antibodies in their blood – even though only 15.1% reported contact with cases ([J Infect Dis](#)).

An experimental vaccine for Crimean-Congo hemorrhagic fever virus is effective in macaques ([EurekAlert](#)).

#### *Odds and Ends*

A 102-year-old New York woman, who lived through the 1918 Spanish flu pandemic, has now beaten COVID-19... twice ([NBC](#)).

"Can dogs smell COVID? Here's what the science says" ([Nature](#)).

Dr. Fauci says Santa has 'innate immunity' ([USA Today](#)). Maybe he got herd immunity from his reindeer, since they are one of mammals found to have a high propensity for binding SARS-CoV-2 ([PNAS](#)).

And speaking of Dr. Fauci... if you ever think your schedule is hectic, take a look at his ([HuffPost](#)).

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